10/088857

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70) 12

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
GELOG 1 WO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US00/26207	25/09/2000	23/09/1999
International Patent Classification (IPC) or national classification and IPC C12Q1/68		
Applicant GENE LOGIC, INC. et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
16/03/2001	23.01.2002
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Wieser, M Telephone No. +49 89 2399 8434

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/26207

I. Basis f th rep rt

1. With regard to the **lements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-64 as originally filed

Claims, No.:

1-38 as originally filed

Drawings, sheets:

1/5-5/5 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	21-28
	No:	Claims	1-20,29-38
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-38
Industrial applicability (IA)	Yes:	Claims	1-38
	No:	Claims	

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

S cti n V

D1: WO 97 42345 A (ZENECA LTD ;WHITCOMBE DAVID MARK (GB); LITTLE STEPHEN (GB); BROWNI) 13 November 1997 (1997-11-13)
D2: WO 98 40518 A (GUILFOYLE RICHARD A ;GUO ZHEN (US); WISCONSIN ALUMNI RES FOUND (US) 17 September 1998 (1998-09-17)
D3: WO 97 14028 A (LUMINEX CORP ;CHANDLER VAN S (US); FULTON R JERROLD (US); CHANDLER) 17 April 1997 (1997-04-17)
D4: WO 98 10095 A (BRAX GENOMICS LTD ;THOMPSON ANDREW HUGIN (GB); SCHMIDT GUNTER (GB)) 12 March 1998 (1998-03-12)

1. **Claims 1-28**

1.1. D1 (see pages 1,6,12 and 13; claims and fig.17) refers to a method for detecting a nucleic acid base sequence, comprising mutation specific extension of tagged primers. The products are detected with primers against the tag and with the help of TagMan probes. The binding region of the TagMan probe can be introduced via the allele-specific primer. These allele-specific primers clearly fall within the definition of an "indexing reagent" as given in the present application. Therefore, the disclosure in D1 anticipates the subject-matter of claims 1-20, which does not meet the requirements of Article 33(2) PCT.

Due to the generic and broad wording of the independent claims, also the disclosure in D3 (see abstract and claims) is anticipating claims 1-4 and 8-20.

1.2. The specific indexing methods of claims 21-28, which refer back to claims 1-4, are distinguished from the disclosure in D2 (see claims) insofar, as D2 does not disclose homogenous detection, but relies on size separation by gel electrophoresis. The problem to be solved by the underlying invention is therefore, as described on pages 5-6 of the description, the provision of simple, relatively fast and easy to automate methods that overcome the disadvantages of electrophoretic separations.

Quantitative real time PCR using TagMan probes is a method known in the art, which has been exclusively designed to overcome the above problems. A person

skilled in the art, when trying to solve this problem, would turn to D1 where exactly this method is described. When combining the teaching of D1 and D2 he/she would arrive at the claimed subject-matter in an obvious way. Accordingly, claims 21-28 are not based on an inventive concept and do not meet the requirements of Article 33(3) PCT.

2. **Claims 29-38**

The devices necessary for carrying out the methods described in D2 and D4 (see examples) contain all technically characterising features of the device according to claims 29-38. Moreover, also documents D1 and D3 are considered to anticipate the device of claims 29-36.

The claims are not novel and do not meet he requirements of Article 33(2) PCT.

Section VIII

The scope of protection conferred by a patent is defined in the claims. The term "paragraph(s)" as used throughout the claims should therefore be deleted. Moreover, the second set of claims ("paragraphs") contained in the description (pages 7-12) is misleading and has to be deleted.

The term "Type 11 restriction cite" in claim 28 is not clear (Art.6 PCT).

Citations of prior art documents "being hereby incorporated by reference" should be deleted.

PATENT COOPERATION TREATY

PCT

10/088857

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
GELOG 1 WO		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US 00/ 26207	25/09/2000	23/09/1999
Applicant		
GENE LOGIC, INC.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 1

   [ ] as suggested by the applicant.

   [X] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [ ] None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
T/US 00/26207

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, MEDLINE, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 42345 A (ZENECA LTD ;WHITCOMBE DAVID MARK (GB); LITTLE STEPHEN (GB); BROWNI) 13 November 1997 (1997-11-13)	1-20, 29-36
Y	page 1 page 12-13 page 6; claims; figure 17	21-28

X	WO 98 40518 A (GUILFOYLE RICHARD A ;GUO ZHEN (US); WISCONSIN ALUMNI RES FOUND (US) 17 September 1998 (1998-09-17)	29-38
Y	the whole document	21-28

X	WO 97 14028 A (LUMINEX CORP ;CHANDLER VAN S (US); FULTON R JERROLD (US); CHANDLER) 17 April 1997 (1997-04-17) page 1-12 page 87-109	1-4, 8-24, 29-36

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 June 2001	28/06/2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Reuter, U

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Form PCT/ISA/210 (second sheet) (July 1992)

International Application No
[redacted]T/US 00/26207

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 10095 A (BRAX GENOMICS LTD ;THOMPSON ANDREW HUGIN (GB); SCHMIDT GUNTER (GB)) 12 March 1998 (1998-03-12) page 21-26 page 32-35; figure 6 ---	29-38
A	EP 0 735 144 A (JAPAN RES DEV CORP) 2 October 1996 (1996-10-02) the whole document ---	1-38
A	UNRAU P ET AL: "NON-CLONING AMPLIFICATION OF SPECIFIC DNA FRAGMENTS FROM WHOLE GENOMIC DNA DIGEST USING DNA 'INDEXERS'" GENE, 1994, XP002054436 the whole document ---	1-38
A	WO 97 31256 A (BLOK HERMAN ;BARANY GEORGE (US); KEMPE MARIA (US); ZIRVI MONIB (US) 28 August 1997 (1997-08-28) the whole document ---	1-38
A	WO 99 02727 A (BRAX GENOMICS LTD ;THOMPSON ANDREW HUGIN (GB); SCHMIDT GUENTER (GB) 21 January 1999 (1999-01-21) the whole document -----	1-38

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
T/US 00/26207

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9742345 A	13-11-1997	AU 2704997 A	26-11-1997
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		JP 2000510337 T	15-08-2000
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		AU 7465198 A	29-09-1998
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		EP 0920440 A	09-06-1999
WO 9902727 A	21-01-1999	AU 8234798 A	08-02-1999
		AU 8234998 A	08-02-1999
		EP 0994967 A	26-04-2000
		EP 0994969 A	26-04-2000
		WO 9902725 A	21-01-1999

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
29 March 2001 (29.03.2001)

PCT

(10) International Publication Number
WO 01/21840 A3

(51) International Patent Classification[7]: C12Q 1/68

(21) International Application Number: PCT/US00/26207

(22) International Filing Date:
25 September 2000 (25.09.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/155,488 23 September 1999 (23.09.1999) US

(63) Related by continuation (CON) or continuation-in-part (CIP) to earlier application:
US 60/155,488 (CIP)
Filed on 23 September 1999 (23.09.1999)

(71) Applicant *(for all designated States except US)*: GENE LOGIC, INC. [US/US]; 708 Quince Orchard Road, Gaithersburg, MD 20878 (US).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: GUILFOYLE, Richard [US/US]; 11408 Scottsbury Terrace, Germantown, MD 20876 (US).

(74) Agents: ZELANO, Anthony, J. et al.; Millen, White, Zelano & Branigan, P.C., Arlington Courthouse Plaza 1, 2200 Clarendon Boulevard, Suite 1400, Arlington, VA 22201 (US).

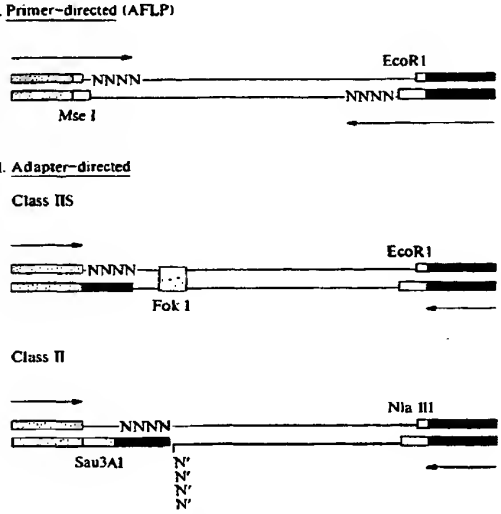
(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

[Continued on next page]

(54) Title: INDEXING POPULATIONS



(57) Abstract: The invention relates to method and devices for indexing populations, among other things. Particular embodiments relate to methods for indexing population that can be carried out in homogeneous media, particularly methods in which indexing reactions can be carried out in homogeneous media and the products of the reactions can be determined without physically separating the products from the reaction. In these and other regards the invention further relates to methods and devices for indexing using real time monitoring and determinations based on reaction kinetics. In another further respect in these and other regards the invention relates to multiplexed indexing. And, in a still further specific in all these regards the invention relates to methods and devices for indexing a substantial fraction of all sub-populations of a given type. Specific embodiments relate to polynucleotides to expression profiling and to strand displacement indexing and reagent for strand displacement indexing.

WO 01/21840 A3

(88) Date of publication of the international search report:
6 December 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.